Development of ^{52g}Mn for Diagnostic Applications in Positron Emission Tomography at UW-Madison

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Introduction

Interests in positron emission tomography (PET) applications of manganese radionuclides have been motivating further studies in ^{52g}Mn production, separation and labeling.

The production of ^{52g}Mn ($t_{1/2}$ = 5.591 d, $I_{\beta+}$ = 29.4%, $E_{\beta,avg}$ = 241.6 keV) via the ^{nat}Cr(p,x)^{52g}Mn pathway is routinely carried out at UW Madison's low-energy cyclotron[1]. After irradiation, the residual chromium target material and other trace metals must be removed. Impurities could negatively impact the effectiveness of labeling and inhibit further biological studies due to excess toxicity.

While ^{52g}Mn labeling has been achieved with chelating agent DOTA, the promising potential of Mn-specific chelators and other chelators of high biostability are still under research.

Methods

- Production

Natural chromium was electroplated or hydraulically pressed onto silver disks to create targets for 12-16 MeV proton irradiation at the GE PETtrace cyclotron. (See Fig. 1.)

Figure 1. Electroplated ^{nat}Cr target. In collaboration with Dr. M. Chernysheva.

Theoretical calculations, which adopted atomic and nuclear data retrieval and interpolation by python toolkit Curie, were performed for yield predictions[3].

- Separation

After irradiation and letting ^{52m}Mn ($t_{1/2}$ = 21.1 min, E_γ = 1434.06 keV) decay, the target was dissolved and ^{52g}Mn was separated from the solution[1]. The separation process is summarized in Fig. 2. The Actinide Resin™ chosen has relatively higher affinity for Mn^{2+} than for Cr^{3+} in HCl of lower than 5 M concentrations, allowing ^{52g}Mn to remain in the columns while target material is removed[4].

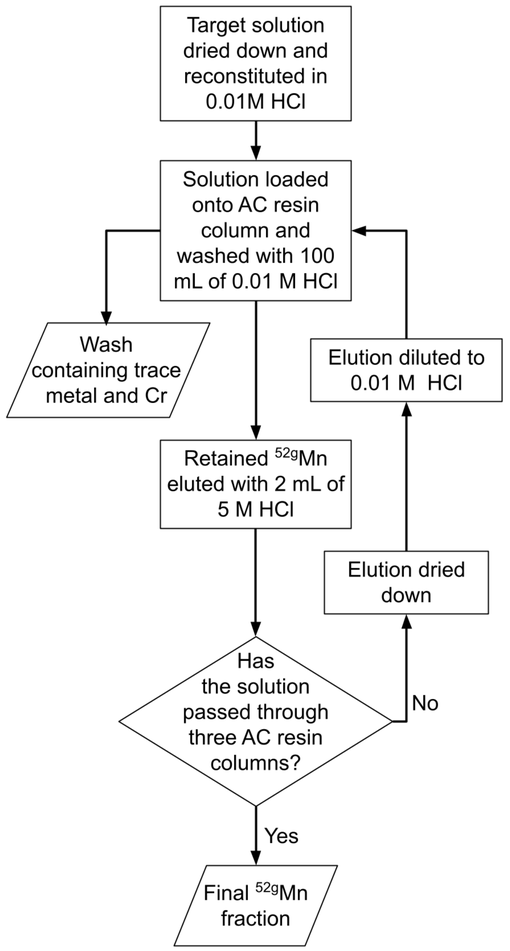

Figure 2. Flow diagram of ^{52g}Mn/^{nat}Cr separation protocol[4].

- Labeling

The purified ^{52g}Mn was labeled with DOTA of various concentrations, allowing data acquisition for apparent molar activity (AMA) calculations. The AMA values served to show whether separation was successful, as DOTA also chelates to the trace mental content[4].

Results

- Production

As seen in Fig. 3, experimental data showed general agreement with theoretical yield calculations performed. The uniformity of electroplated ^{nat}Cr targets allowed relatively accurate predictions.

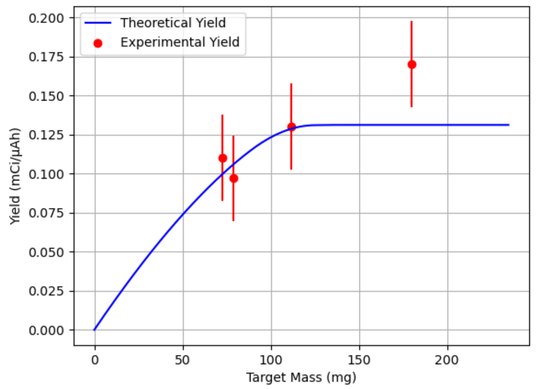

Figure 3. Theoretical and experimental thick target yield of ^{52g}Mn. Experimental yield corrected for beam spread.

- Separation

The purity of the final product was verified by microwave plasma - atomic emission spectroscopy (MP-AES). Table 1 shows that the concentrations of transition metals and chromium contamination were low enough for current needs in biological studies.

Effective DOTA labeling, as shown in the following section, was also an indication of proper removal of impurities.

Table 1. Concentration of trace metals and Cr post-separation (n=1).

Element	Concentration
Zn	2 ppm
Fe	< 50 ppb
Cu	0.4 ppm
Ni	0.1 ppm
Co	1.5 ppm
Cr	0.75 ppm

- Labeling

Thin layer tomography (TLC) was used to assess the labeling results. Fig. 4 features the increasing level of chelation with rising concentrations of DOTA at pH 5.5. The AMA of labeling of ^{52g}Mn with DOTA typically fell above 2 mCi/μmol when using activity of approximately 16 μCi/vial.

Conclusion and Outlook

Current protocols in ^{52g}Mn production and purification from ^{nat}Cr targets had been proven to be effective in producing the isotope of interest in both high yield and purity.

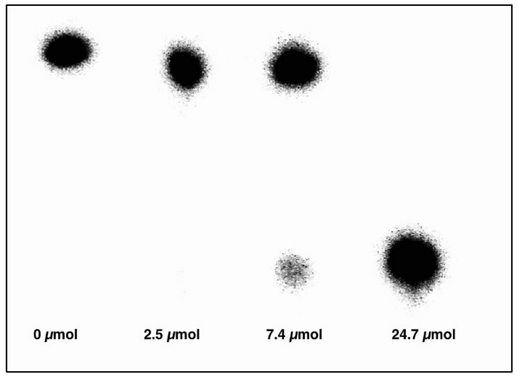

Figure 4. TLC plate.

However, the current production route simultaneously produces chemically inseparable ^{54}Mn ($t_{1/2}$ = 312.20 d, E_γ = 834.848 keV) contamination[2]. The long half-life and high intensity decay gamma-ray makes ^{54}Mn an undesirable by-product that obstructs further clinical research.

Ongoing studies propose target fabrication via electroplating powdered enriched ^{52}Cr, yet recycling remains a problem in establishing a sustainable production pathway.

There remains room for improvement in manganese radionuclide labeling; chelators of stronger bonds or applications for different biological models are still being investigated.

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